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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/931,112	08/17/2001	Marshall Z. Schwartz	06510003PB	3767

7590 07/26/2004

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EXAMINER	
BORIN, MICHAEL L	
ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/931,112	SCHWARTZ, MARSHALL Z.	
	Examiner	Art Unit	
	Michael Borin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,9-12 and 21-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,9-12 and 21-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Examiner acknowledges response filed 04/30/3004. Applicant's arguments have been fully considered and they are deemed to be persuasive. First, Examiner acknowledges that specification does provide support for the term "intestine" (used in the amended claims instead of originally claimed "small intestine"). Second, Examiner agrees that election of species requirement was excessive and hereby vacates the requirement.

Claims pending are 7,9-12, 21-33.

Claim Rejections - 35 U.S.C. § 103

2. Claims 7,9-12, 21-33 are rejected under 35 U.S.C. 103(a) as being obvious over Zushi and Ishii and Fukamachi and Halttunen. The rejection is maintained for the reasons of record as applied to claims 7-12 in the first Office action on merits.

Response to arguments

Applicants have traversed the references pointing to the differences between the claims and the disclosure in each reference. Applicant is respectfully reminded that the rejection is under 35 USC103 and that unobviousness cannot be established by attacking the references individually when the rejection is based on the

combination of the references. It has been well established that the test for combining references is not what individual references themselves suggest but what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art. *In re McLaughlin,* 170 USPQ 209 (CCPA 1970).

Applicant argues that as all the referenced studies are *in vitro*, their results can not be translated to *in vivo* effects. The rejection combined several references to demonstrate that HGF has similar proliferative effect on different cell systems each of which is an adequate model of *in vivo* conditions. For example, Zushi reference teaches that "Caca-2 cell line has been extensively used as a model of differentiated normal intestinal epithelium in examination of the mechanisms of absorption, electrolyte transport, and restitution" (p.G757, right column, end of second paragraph). *In vitro* testing may establish a practical utility of a compound if *in vitro* data are reasonably predictive of the therapeutic utility. The cell models described in the references are all accepted as reasonably correlated to the *in vivo* conditions and pharmacological activity is reasonably based on the probative evidence. The applicant has not provided any evidence that the *in vitro* observations can not be reasonably correlated to *in vivo* effects.

Applicant argues that neither of the references teaches increase in the intestinal absorptive functions and intestinal mass. Applicant acknowledges that the references

teach that the references teach that HGF provides for proliferation, growth and motility of intestinal cells. The references used in the rejection demonstrate that HGF causes proliferation of intestinal cells. Proliferation of intestinal cell will be manifested in an increase in intestinal tissue mass and will result in an increase in intestinal absorptive functions. This is because intestinal absorption is a result of combination of multiple molecular transport mechanisms operating in intestinal cells. Each intestinal cell has a finite transport capability, and consequently, intestinal absorption capability is determined, in part, by the amount of intestinal cells in the intestine. Therefore, an increase in the amount of intestinal cells will result in an increase in their total absorptive capability, and it would be obvious to expect that proliferation of the intestinal cells will cause an increase in the intestinal absorptive functions. In addition, proliferation of intestinal cells will, naturally, result in an increase in intestinal tissue mass. As there is a need, for certain disorder conditions, to increase intestinal absorptive functions and/or intestinal tissue mass, a practitioner would be motivated to use HGF to achieve these desired effects because *in vitro* studies on adequate models strongly suggest that HGF would cause proliferation and growth of intestinal cells *in vivo.*

Next, applicant argues that the dosage range would not have been obvious. As stated in the rejection, absent teaching to the contrary, the determination of particular ranges employed is within the skill of the ordinary worker as a part of the

process of normal optimization. Applicant did not provide any factual evidence to demonstrate unexpected results achieved by using the claimed dosage range. Attorney arguments is not evidence unless it is an admission. The arguments of counsel can not take the place of evidence in the record.

Further, applicant argues that it is assumed by Examiner that the only primary mechanism of action of HGF is through cellular proliferation. Without addressing the merits of such argument, the instant claims are not drawn to any particular cellular mechanism.

Further, applicant refers to previously allowed parent application 08/932391 and argues that similar art rejection was considered to be moot in that case. Note, however, that after discussing the claimed subject matter in the parent case, applicant agreed to limit claim language to an embodiment of increasing intestinal absorbtive functions and intestinal tissue mass beyond the normal adaptive response. This is not the case in the instant application.

Double Patenting

3. Claims 7,9-12, 21-33 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 5972887. The rejection is maintained for the reasons of record as applied

to claims 7-12 in the first Office action on merits. It is noted that applicant intends to file a Terminal Disclaimer upon identification of allowable subject matter.

Conclusion.

4. No claims are allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are

unsuccessful, the examiner's supervisor, Mr. Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0549.

July 22, 2004

MICHAEL BORIN, PH.D
PRIMARY EXAMINER

mlb